REMARKS

Claims 2-10, 27-31 and 33-37 are pending and under examination in the above-identified application. Applicants have reviewed the rejections set forth in the Office Action mailed March 8, 2006, and respectfully traverse all grounds for the reasons that follow.

Applicants would like to thank Examiner Strzelecka for extending a personal interview with Applicants' representatives on August 22, 2006. The amendments above and remarks below are believed by Applicants to substantially conform to the subject matter discussed in the interview. Applicants respectfully request reconsideration and withdrawal of all grounds of rejections based on the discussions of the interview and the remarks herein.

Rejections Under 35 U.S.C. § 102

Claims 2, 5-9, 27-31 and 33-37 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Kuimelis et al. (U.S. Patent No. 6,537,749). The Office alleges that Kuimelis et al. describe the synthesis and cleaving of first and second linkers to release oligonucleotides from a support, and therefore, inherently describes creating the pools of oligonucleotides. Lashkari et al. is cited in support for allegedly describing oligonucleotide synthesis.

When lack of novelty is based on a printed publication that is asserted to describe the same invention, a finding of anticipation requires that the publication describe all of the elements of the claims. *C.R. Bard, Inc. v. M3 Sys., Inc.*, 157 F.3d 1340, 1349, 48 U.S.P.Q.2d 1225, (Fed. Cir. 1998) (quoting *Shearing v. Iolab Corp.*, 975 F.2d 1541, 1544-45, 24 U.S.P.Q.2d 1133, 1136 (Fed. Cir. 1992)). To establish a *prima facie* case of anticipation, the Office must show that the single reference cited as anticipatory art describes all the elements of the claimed invention.

Applicants respectfully submit that Kuimelis et al. fails to describe all elements of the claimed invention because Kuimelis et al. does not teach - expressly or inherently - release of oligonucleotides to create a pool of different oligonucleotides as is claimed by the invention. The Office cites to col. 10, lines 20-25; col. 12, lines 45-49, and col. 15, lines 64-67, for allegedly supporting creation of a pool of oligonucleotides. These passages describe general oligonucleotide synthesis and state, in relevant part, that synthesized oligonucleotides are released. The mere description of releasing synthesized products from a solid phase does not

describe release of different products to form a pool. As set forth below, the description in Kuimelis is directed to release of individual products and purification from impurities generated during synthesis. In particular, Kuimelis et al., under the heading entitled "Synthesis of Capture Probes" describe at column 10:

> Capture probe sequences are cleaved from the solid support and deprotected with ammonium hydroxide, concentrated to dryness, precipitated in ethanol, and purified by reverse-phase HPLC using acetonitrile gradient in triethylammonium acetate buffer.

Id., at lines 20-25 (emphasis added).

Similar descriptions are cited at column 12, lines 45-49, where Kuimelis et al. describe:

> All capture oligo sequences were cleaved from the solid support and deprotected with ammonium hydroxide, concentrated to dryness, precipitated in ethanol, and purified by reverse-phase HPLC using an acetonitrile gradient in triethylammonium acetate buffer.

Id. (emphasis added).

Further, at column 15, Kuimelis et al. also describe:

> Capture oligo sequences were cleaved from the solid support and deprotected with ammonium hydroxide, concentrated to dryness, precipitated in ethanol, and purified by reverse-phase HPLC using an acetonitrile [gradient].

Id., at lines 64-67 (emphasis added).

As shown above, there are no descriptions that the synthesized oligonucleotide are released into a common mixture to create a pool. In contrast, the above descriptions and throughout the rest of Kuimelis et al., teach just the opposite - namely, that the oligonucleotides are not combined into a mixture because Kuimelis et al. expressly describes that all of the synthesized oligonucleotides are purified by reverse-phase HPLC.

Furthermore, there are no descriptions in Kuimelis et al. that the synthesized oligonucleotide, once purified, are in any way combined into a common mixture to create a pool. The invention claims generating a pool of oligonucleotides comprising first and second different oligonucleotides. For example, step (b) of claim 27 recites cleaving to release the first and

second linkers to thereby generate a pool of oligonucleotides having first and second different oligonucleotides. Further, the application describes at, for example, in the paragraph bridging pages 8 and 9, that the term "pool" is intended to refer to "a plurality or more than one solution-phase oligonucleotide," and that a pool preferably includes "two or more different oligonucleotides." Therefore, Applicant has described and further expressly claimed that a pool constitutes a mixture of different solution-phase oligonucleotides. Such a pool is distinct from Kuimelis et al. which expressly teaches purifying the individual oligonucleotides once released and then attaching the oligonucleotides to a solid phase support, whereby they are no longer in solution-phase.

As discussed during the interview, any postulation that the synthesized oligonucleotides of Kuimelis et al. can hypothetically be combined at some attenuated time is mere speculation and is insufficient to meet the test for anticipation under § 102. The postulation that such a step may (or may not) be possible does not cure the requirement that the four corners of the 102 reference must teach each and every element. Kuimelis et al. fails to satisfy this requirement because it does not describe releasing a mixture of different oligonucleotides to create pool of different oligonucleotides as claimed by the invention.

In light of the discussions during the interview and Applicants' remarks above, Applicants maintain that the claimed invention is distinct from Kuimelis and respectfully request withdrawal of this ground of rejection.

Rejections Under 35 U.S.C. § 103

Claims 2, 5-9, 27-31 and 33-37 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Holmes, U.S. Patent No. 5,679,773, and Beattie, U.S. Patent No. 6,156,502. The Office maintains that it would have been obvious to use the oligonucleotide fingerprinting assay described by Beattie with the method of synthesis and release of nucleic acids from Holmes to arrive at the claimed invention. In particular, the Office alleges that Holmes describes the synthesis and release of oligonucleotides to generate at least two oligonucleotides in a pool. In support, the Office states:

> However, as explained in several of the previous office actions, Applicants definition of a pool encompasses any two oligonucleotides.

Office Action mailed March 8, 2006, p.2, para. 4, last complete sentence (emphasis added).

The Office further alleges Holmes describes that the released oligonucleotides can be used in subsequent bioassays, which provides the rational for oligonucleotide release, and that Beattie further describes cleaving oligonucleotides from a support. The Office further expressly concludes:

> [B]oth Holmes and Beattie et al. provide specific teaching of creating of pools of oligonucleotides according to Applicant's definition, and a rationale for cleaving the oligonucleotides from their supports.

Office Action mailed March 8, 2006, p.4, para. 3 (emphasis added).

Where an invention is contended to be obvious based upon a combination of elements across different references, the Federal Circuit case law "require that there be a suggestion, motivation or teaching to those skilled in the art for such a combination." *Iron Grip Barbell, Co. v. York Barbell, Co.*, Case No. 04-1149, slip op. at 5 (Fed. Cir. December 14, 2004) (citing *In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988)). This requirement prevents the use of "the inventor's disclosure as a blueprint for piecing together the prior art to defeat patentability—the essence of hindsight." *Id.* (citing *Ecolochem, Inc. v. So. Cal. Edison Co.*, 227 F.3d 1361, 1371-72 (Fed. Cir. 2000) (quoting *In re Dembiczak*, 175 F.3d 994, 999 (Fed. Cir. 1999) (abrogated on other grounds))

Applicants respectfully maintain that the cited combination of Holmes and Beattie neither teach, suggest or provide the requisite motivation to arrive at the claimed invention because Holmes and Beattie fail to suggest a pool of oligonucleotides as claimed. While Holmes and Beattie describe the release of oligonucleotides from a synthesis support, the resultant oligonucleotides fail to correspond to Applicants' claimed pool of oligonucleotides.

In particular, the Office correctly concludes that the application defines a pool to include two or more oligonucleotides. However, the Office appears to overlook that the definition includes two or more different oligonucleotides. In particular, and as set forth above under the § 102 rejection, the application defines a pool to mean:

> [A] plurality or more than one solution-phase oligonucleotide. Preferably, a pool includes two or more different oligonucleotides. More preferably a pool includes

> 20 or more different oligonucleotides. Most preferably a pool includes greater than 50 different oligonucleotides.

Application at paragraph bridging pages 8-9 (emphasis added).

Applicants have expressly claimed the release of different first and second oligonucleotides to generate a pool having different first and second oligonucleotides. Therefore, the Office's claim interpretation based on the first sentence of the term's definition is over inclusive and incorrect because the claims expressly recite that the population includes different oligonucleotides within the claimed pool. Therefore, the cited combination of Holmes and Beattie fails to render the invention obvious because they do not teach, suggest or provide the requisite motivation to arrive at all elements of the claimed invention - namely, the generation of a pool of different oligonucleotides.

Further with respect to the alleged rationale that release of the oligonucleotides in Holmes is for use in subsequent bioassays, Applicants' respectfully point out that these descriptions are under the section entitled "Novel Linking Groups" and are directed to the characterization of ligands in binding experiments (see, for example, col. 11, line 10, and the Office's citation at col. 12, lines 6-16). In particular, Holmes expressly state:

> In one application, these linking groups can be used for the photoinduced release of oligomers or small ligand molecules from a surface for characterization purposes following a bioassay.

Id., col. 12, lines 9-13 (emphasis added).

There is no teaching or suggestion in Holmes that the characterization of binding activity involves a pool of different solution-phase oligonucleotides. Rather, binding characterizations generally involve determining the binding activity between a ligand and receptor either in discrete vessels or at discrete locations on solid-phase. Therefore, there is no apparent connection between the release of certain ligands for characterization studies and any arrays described in Holmes containing different oligonucleotides. In contrast, the arrays in Holmes are described as being useful for diagnostic purposes (see, for example, col. 2, lines 13-16) whereas the linking groups are associated with release of oligomers or small ligands from a surface "for characterization purposes following a bioassay" (col. 12, lines 11-13, emphasis added). Hence,

any alleged rationale in Holmes for combining its descriptions with Beattie are absent because Holmes describe use of oligonucleotides in distinct sites, but further describes that any release of oligomers or small ligands is for characterization purposes. Absent any showing that characterization is taught or suggested to be performed on a pool of different oligonucleotides, Applicants submit that the requisite motivation to combine is lacking.

Accordingly, Applicants respectfully submit that the cited combination of Holmes and Beattie fails to render the invention obvious because they do not teach, suggest or provide the requisite motivation to arrive at the generation of a pool of different oligonucleotides. Similarly, as with the § 102 rejection and as discussed during the personal interview, any postulation that the released oligonucleotides can hypothetically be combined at some attenuated time is mere speculation and is insufficient to teach or suggest generating a pool of different oligonucleotides as is claimed. Such speculation does not cure the requirement that all elements of the claimed invention must be taught or suggested in the cited combination of references. In light of the above remarks and the personal interview with Examiner Strzelecka, Applicants respectfully request that this ground of rejection be withdrawn.

CONCLUSION

Applicant submits that the claims are in condition for allowance and respectfully request a notice to this effect. Should the Examiner have any questions, she is invited to call the undersigned attorney.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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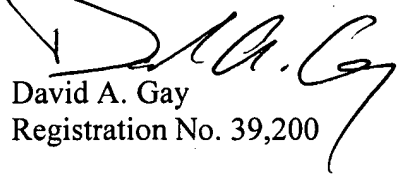

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